Please amend claims 1, 5, 6, 8, 10, 11, 16 and 20 to read as follows. A marked-up copy of claims 1, 5, 6, 8, 10, 11, 16 and 20, showing the changes made thereto, is attached.

1. (Twice Amended) A method for screening of the presence or absence of variation in a portion of a test nucleic acid comprising the steps of:

(a) providing a DNA array substrate by:

i) preparing a substrate;

ii) preparing a group of probes, each probe having a base sequence that hybridizes with a wild-type sequence of the portion to give a strong signal;

iii) preparing a group of probes, each probe having a base sequence that is expected to hybridize with a gene variant but not with the wild-type sequence to give a strong signal; and

C4

iv) fixing each group of probes in separate regions of the substrate;

(b) reacting the test nucleic acid with the probes on the DNA array substrate;

(c) measuring a signal intensity of each region as a total of signals originating from respective hybrids formed between the test nucleic acid and the probes to obtain a histogram pattern of signal intensity of the regions; and

(d) determining the presence or absence of mutation in the test nucleic acid comparing with the histogram pattern with a histogram pattern obtained using an array substrate obtained by step (a) and a reference nucleic acid having the wild-type sequence.

5. (Twice Amended) The method according to claim 1, wherein the steps (a-iv) to (d) further comprise:

C5

(a-iv) preparing separate regions on a substrate by fixing probes on a surface of the substrate, wherein the separate regions comprise:

a first region containing probes which provide a signal of a certain intensity on reaction with a reference nucleic acid having the wild-type sequence,

a second region containing probes which provide weaker signals on reaction with the reference nucleic acid, and

a third region containing probes which do not form hybrids on reaction with the reference nucleic acid;

(b and c) reacting the DNA array of step (a) with the reference nucleic acid and measuring a signal of at least one region selected from the three regions to obtain a first pattern;

C5 cont.

(b' and c') reacting the DNA array of step (a) with the test nucleic acid and measuring a signal of at least one region corresponding to the at least one region selected in step (b and c) to obtain a second pattern; and

(d) determining the presence or absence of variation in the test nucleic acid by comparing the first and second patterns.

6. (Twice Amended) The method according to claim 5, wherein the at least one region selected in step (b and c) is the first region giving a strongest total signal and/or the third region giving no or a weakest signal on reaction with the reference nucleic acid.

C6

8. (Amended) The method according to claim 5, wherein the at least one region selected in step (b and c) is the third region and the test nucleic acid is determined to have variation when the signal is detected in the third region with the test nucleic acid in step (b' and c').

C7

10. (Amended) The method according to claim 5, wherein the at least one region selected in step (b and c) are both the first and the third region and determining the

presence or absence of variation is determined by comparing the ratio of the intensity of the third region to that of the first region.

C7 cont.

11. (Twice Amended) The method according to claim 5, wherein all three regions are selected in step (b and c) and the presence or absence of variation is determined by comparing the histogram pattern of signal intensity.

16. (Twice Amended) A DNA array substrate for screening variation in a portion of a nucleic acid comprising:

a first group of probes, each probe having a base sequence that hybridizes with a wild-type sequence of the portion to give a strong signal, and

a second group of probes, each probe having a base sequence that is expected to hybridize with a gene variant but not with the wild-type sequence to give a strong signal;

C8

wherein the probes are arranged on a substrate to form at least two separate regions selected from:

a first region containing probes of the first group,

a second region containing probes of the second group, each of which provides a weaker signal than the probes of the first region on reaction with the wild-type sequence, and

a third region containing probes of the second group, each of which provides no signal on reaction with the wild-type sequence.

C9

20. (Twice Amended) The DNA array substrate according to claim 16, wherein the separate regions are arranged on the substrate in order of signal intensity obtainable by reacting with the wild-type sequence along a direction of a detection.